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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/590,284	06/09/2000	David M. Goldenberg	018733-0967	3453

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HELLER EHRMAN WHITE & MCAULIFFE LLP
1666 K STREET,NW
SUITE 300
WASHINGTON, DC 20006

EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/590,284	GOLDENBERG ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-80* is/are pending in the application.

4a) Of the above claim(s) *44,54-74 and 77-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43, 45-53, 75, and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's reply, filed 10/13/2004, is acknowledged and has been entered.

Claims 1 – 38 and 81 – 106 have been cancelled previously.

Claims 39 – 80 are pending.

Claims 44, 54 – 74, and 77 – 80 have been withdrawn from consideration as being drawn to nonelected species.

Claims 39 – 43, 45 – 53, 75, and 76 are under consideration in the instant application.

2. It is noted that the claims, as limited to previously elected species, are considered for the purposes of examination to be drawn to a method of treating multiple sclerosis comprising administering a therapeutic composition comprising a naked anti-CD20 antibody, a naked anti-CD22 epitope B antibody, and the cytokine IFN-β (instant claims 75 - 76).

3. This Office Action will be in response to applicant's arguments, filed 10/13/2004.

The rejections of record can be found in the previous Office Action.

The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

4. Claims 39 – 43, 45 – 53, 75, and 76 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bhat et al. (US Pat. 5,593,676, see entire document) in view of Tedder et al. (US Pat. 5,484,892, of record, see entire document), and further in view of Anderson et al. (US Pat. 5,776,456, of record, see entire document) and Goldenberg (US Pat. 6,306,393, see entire document).

Applicant's arguments have been fully considered but were found only partially convincing.

Applicant argues that the rejection fails to satisfy a two-part test for obviousness because Bhat et al. do not provide sufficient motivation to make the combination or a reasonable expectation that the combination would succeed. Applicant provides references to show that the specific antibody taught by Bhat et al. is not limited in specificity to B cells.

Applicant's arguments are acknowledged, however, as detailed below, (a) the teachings of Bhat et al. are not limited to the use of one specific antibody, and (b) the motivation and expectation of success are also provided by the other cited references.

a). Bhat et al. teach: "Methods are provided for inducing cell death in B-cells ... by employing reagents that bind to a B-cell marker" (column 2 lines 7 – 9). Bhat et al. further exemplify "surface membrane protein markers found on normal B-cells, such as CD19, CD20, CD21 and CD22" (column 2 lines 25 – 27). Thus the teachings of Bhat et al. are not limited to the use of one particular antibody for B cell depletion.

Further, when viewed in the context of the entire document, the following passage from Bhat et al. clearly refers to motivation for depleting B cells in autoimmune disease: "...Autoimmune diseases can be extremely destructive, as is evidenced by diabetes, rheumatoid arthritis, neuronal diseases, such as multiple sclerosis, and the like. While in many cases, the disease is associated with T-cell attack, in some of the diseases, there may be a B-cell component" (column 1 lines 33 – 38).

b). The motivation to combine antibodies to either CD20 or CD22 with other antibodies or with each other, and a reasonable expectation of success of such combinations for treating the respective conditions, including autoimmune disorders, are found in Tedder et al. (see entire document, in particular, column 6), Anderson et al. (see entire document, in particular, columns 29 – 32), and Goldenberg et al. (see entire document, in particular, column 19).

Therefore the combined references make out a *prima facie* case of obviousness. The rejection is maintained for the reasons of record. The rejection of record is reiterated below for Applicant's convenience.

> The claims are drawn to a method of treating multiple sclerosis comprising administering a therapeutic composition comprising a naked anti-CD20 antibody, a naked anti-CD22 epitope B antibody, and the cytokine IFN-β.
>
> Bhat et al teach methods of depleting B cells by administering to a host antibodies which bind B cell markers (column 2 lines 6 – 13), such as CD19, CD20 and CD22 (column 2 lines 24 – 27). Bhat et al contemplate using these methods to treat autoimmune diseases, such as multiple sclerosis (column 1 lines 33 – 36).
>
> Bhat et al do not teach the use of a combination of anti-CD20 antibody, anti-CD22 epitope B antibody, and IFN-β.

Tedder et al teach the use of anti-CD22 antibodies, including those reacting with epitope B (column 2, lines 26 – 42 and column 11, table III), for treatment of various autoimmune disorders (e.g. column 3 2nd paragraph). Tedder et al also teach the use of anti-CD22 antibodies in combination with other antibodies or agents (column 6 lines 55 – 65).

Anderson et al teach the use of anti-CD20 antibody to deplete non-malignant B cells in vivo (see example III, column 24), alone or in combination with other antibodies or agents (columns 29 – 32).

Goldenberg teaches methods of depleting B cells in malignancies by administering various combinations of naked anti-CD19, anti-CD20, and anti-CD22 antibodies (claims 1 and 9), with or without IFNβ (claim 8). One of the anti-CD22 antibodies taught by Goldenberg is LL2 (claim 12), which binds with epitope B of the CD22 antigen, as disclosed on page 14 3rd paragraph of the instant application. Goldenberg teaches a marked depletion of malignant B cells by these treatments (see Examples, columns 17 – 21). Further, Goldenberg teaches that the use of combination of antibodies results in superior treatment compared to anti-CD20 antibodies alone (see e.g. Abstract and Example 2, column 19).

Given the teachings of Bhat et al that administering antibodies to CD19, CD20, and CD22 can lead to depletion of B cells and treatment of multiple sclerosis, the teachings of Tedder et al that administering anti-CD22 epitope B in combination with other antibodies can treat autoimmune disorders, the teachings of Anderson et al that that administering anti-CD20 in combination with other antibodies can deplete B cells in vivo, and teachings of Goldenberg that a combination of anti-CD20 antibodies with either ant-CD19 or anti-CD22 results in a more successful depletion of malignant B-cells, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the above teachings to deplete the population of B cells in a patient by using a combination of the cited antibodies and a cytokine, thus arriving at the claimed invention of treating multiple sclerosis by administering a naked anti-CD20 antibody, a naked anti-CD22 epitope B antibody, and IFN-β.

Furthermore, the ordinary artisan would have been motivated to use a combination of anti-B cell antibodies and a cytokine, as taught by Goldenberg, with a reasonable expectation of success that such combination would be effective in depleting B cells, as taught by Goldenberg and Anderson et al, and would be useful in treating autoimmune disorders, as taught by Tedder et al, including multiple sclerosis, as taught by Bhat et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Conclusion: No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

December 21, 2004

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
12/23/04